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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/099,830	03/13/2002	Philip John Burke	ERD 100 CON	4061

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EXAMINER	
FETTEROLF, BRANDON J	
ART UNIT	**PAPER NUMBER**
1642	

DATE MAILED: 01/18/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/099,830	BURKE ET AL.	
	Examiner	Art Unit	
	Brandon J Fetterolf, PhD	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 November 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *34,41-44,46 and 47* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *34,41-44 and 46* is/are rejected.

7)☒ Claim(s) *47* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The Amendment filed on 11/18/2004 in response to the previous Non-Final Office Action (07/23/2004) is acknowledged and has been entered.

Claims 34, 41-44 and 46-47 are currently pending under consideration.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

Rejections Maintained:

Claims 34 and 41-44 **remain** rejected and new claim 46 are rejected under 35 USC 112, first paragraph, because the specification, while being enabling for a system comprising the prodrug CB 1945 which is converted to a substantially cytotoxic drug by the action of NQO2 and a compound of formula I, does not reasonably provide enablement for system as broadly claimed for the reasons of record (Pages 4-5) in the Action mailed 07/23/2004 and for the reasons set forth below.

In reference to the previous action which held that the specification does not provide enablement for any and all prodrugs which can be converted to a cytotoxic drug by the action of NQO2, Applicants contend (Remarks, 11/18/2004, page 7) that the claims as amended define a "therapeutic system that contains **a prodrug that is converted to a substantially cytotoxic drug by the action of NQO2 and a compound of formula I**" and that this "functional" wording places a clear limitation on the scope of the claims. Therefore, Applicants assert that it is clear that prodrugs, which cannot be converted by NQO2 in to a cytotoxic species do not fall within the scope of the claims, but include only those prodrugs that are converted to a substantially cytotoxic drug by the action of NQO2. Furthermore, Applicants submit that the claims as amended do not include any and all prodrugs, because NQO2 is an example of the general class of reductase, which

will only react with certain chemical functional groups to form cytotoxic species. These arguments have been considered but are not found persuasive.

First, the previous rejection was based on an analysis of whether the disclosure, when filed, supported whether any and/or all prodrugs would effectively be converted into a cytotoxic drug by the action of NQO2 as to enable one skilled in the pertinent art to make and use the claimed invention. Applicants have not provided evidence that any and/or all prodrugs would effectively be converted into a cytotoxic drug by the action of NQO2. For example, while Applicants allege that the claims as amended places a clear limitation into the scope of the claims, i.e. a prodrug that is converted to a substantially cytotoxic drug by the action of NQO2, applicants fail to mention where in the specification one of ordinary skill in the art can ascertain what prodrugs can or cannot be converted by NQO2 into a cytotoxic species. Thus, any arguments that the scope of the instant claim as amended is limited to only prodrugs that can be converted to a cytotoxic drug by the action of NQO2 are not pertinent because this says nothing about how to determine which prodrugs are converted to a cytotoxic drug and which are not. Moreover, while the applicants allege that NQO2 is an example of a general class of reductase that will only react with certain chemical functional groups to form cytotoxic species, applicants have not established a correlation between any and all prodrugs comprising a nitro group and the generation of a cytotoxic species by NQO2. Thus, it appears that applicants are implying that any and/or all prodrugs comprising a nitro group can be activated to a cytotoxic species by NQO2.

In reference to the previous action which held that the specification does not provide enablement for any and all analogs of CB 1954 which can be converted to a cytotoxic drug by the action of NQO2, Applicants contend (Remarks, 11/18/2004, page 8) that the specification provides a person of ordinary skill in the art a starting point for identifying not only analogs of CB 1954, but guidance for identifying analogs of CB 1954 that can be converted by NQO2 into a cytotoxic species, i.e. providing the mechanism shown in Figure 1 and the core functional groups and structures that provide activity. Moreover, Applicants submit that the analogs of CB 1954 contain key functional groups, i.e., aziridine ring and nitro group, that have been recognized and described in the specification as providing cytotoxicity following conversion by NQO2. For example, Applicants assert that Khan and Ross, *Chem. Biol. Interactions*, 1 (1969/1970) pp. 27-47 (IDS) and 4 (1971/1972) pp. 11-22 (IDS) disclose that a wide range of analogs of CB 1954 can have significant carcinostatic

effectiveness provided that they contain an aziridine ring. Furthermore, Applicants contend that methods for testing whether a prodrug is converted by the action of NQO2 are disclosed in the specification and that the specification disclosed the effects of CB 1954 and NQO2 and co-substrates on the cytotoxicity of cells. These arguments have been considered but are not found persuasive.

First, the previous rejection was based on an analysis of whether the disclosure, when filed, supported whether any and/or all analogs of CB 1954 would effectively be converted into a cytotoxic drug by the action of NQO2 and not, whether there was guidance on how to identify analogs of CB 1954. Applicants have not provided evidence that any and/or all analogs of CB 1954 would effectively be converted into a cytotoxic drug by the action of NQO2. For example, while Applicants allege that the specification provides guidance, i.e., mechanism of CB 1954 and NQO2 and the core functional groups of CB 1954, for identifying and testing analogs of CB 1954, applicants fail to mention a direct correlation between the conversion of a nitro group by NQO2 and activation to a cytotoxic drug. Moreover, Applicants admit some experimentation may be necessary to determine whether a prodrug is converted to a substantially cytotoxic drug by the action of NQO2 (Remarks, page 9, 2nd paragraph). Furthermore, Applicants assertion that Khan and Ross indicate a wide range of analogs of CB 1954 whcih have significant carcinostatic effectiveness provided that they contain an aziridine ring is not pertinent, because this says nothing about the activation of a CB 1954 analog by NQO2 (see Figure 1). Specifically, a careful review of Khan and Ross does not disclose a nexus between the aziridine ring and activation to a cytotoxic drug by NQO2, nor does the reference suggest a possible mechanism of action.

Thus, applicant's arguments have not been found persuasive and the rejection is maintained.

New Objections:

Claim Objections

Claim 47 is objected to for being dependent from rejected claim 34. Appropriate correction is required.

All other rejections and or objections are withdrawn in view of applicant's amendments and arguments there to.

Therefore, NO claim is allowed.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brandon J Fetterolf, PhD whose telephone number is (571)-272-2919. The examiner can normally be reached on Monday through Friday from 8:30 to 5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeff Siew can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Brandon J Fetterolf, PhD
Examiner
Art Unit 1642

BF

GARY NICKOL
PRIMARY EXAMINER